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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,941	12/13/2004	Alexander Berthold Hendrik Bakker	2578-6723us	7383

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TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
STOICA, ELLY GERALD	
ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
02/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/517,941	BAKKER ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 27-51* is/are pending in the application.

4a) Of the above claim(s) *7-11,13,14,16,27-45,48,49 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 12, 15, 17, 18, 46, and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-6, 12, 15, 17-18, 46 and 48-51) and of the species Seq. Id. Nos.: 22, 27 and 31, in the reply filed on 11/07/2007 is acknowledged.

Claim Objections

2. Claims 3, 4, 5, 46 are objected to because of the following informalities: they contain non-elected species, there being no allowable generic claim. Appropriate correction is required.

Status of the claims

3. In the amendment filed 11/07/2007, Applicant amended claims 1, 3, 5, 11-13, and 40. Claims 7-11, 13, 14, 16, 27-45, and 47 are withdrawn from prosecution as being drawn to non elected inventions. Claims 19-26 were previously canceled. Claims 1-18 and 27- 51 are pending. As a result of the election/restriction, claims 48, 49 and 51 are withdrawn as being drawn to non-elected species. Claims 1-6, 12, 15, 17, 18, 46, and 50 are currently examined.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6, 12, 15, 17, 18 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a genus of human binding molecules comprising agonistic binding molecules capable of binding to and stimulating a human OX40-receptor, wherein the binding molecule may have a synergistic stimulatory effect when co-incubated with OX40-ligand. The binding molecules comprise a complementary determining region comprising an oligopeptide sequence consisting of 10 to 12 amino acids, wherein the oligopeptide sequence is Xaa1-Xaa2-R- Xaa3-Asp-Xaa4, wherein Xaa1 is selected from the group consisting of Ala, Tyr, and Asp, Xaa2 is selected from the group consisting of Asp, Arg and Met, R is selected from the group consisting of a pentapeptide or a heptapeptide, Xaa3 is Phe or Leu, and Xaa4 is Tyr or Ser. The latter binding molecules may also comprise an immunoconjugate comprising at least one tag. The said molecules may be part of a composition with a stabilizing molecule, a pharmaceutical composition with at least one pharmaceutically acceptable excipient and potentially comprising at least one other therapeutic agent.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial

structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims 1, 2, 12 is a functional property of the molecules claimed without any description of the structural requirements. For the claim 46, and the depending claims 15, 17, 18, a partial structure is offered, which covers less than 40% of the structure of the molecule claimed, without any guidance with respect to the identification the rest of the molecule. In the Specification adequate written description is offered for the antibodies denominated in Table 1 (i.e., SC02-008, SC02-009, SC02-010, SC02-011, SC02-012, SC02-021, SC02-022, and SC02-023). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, there is no guidance with regard to the nature of the therapeutic agent that is claimed in claim 18 or nature of the tag in claim 6.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the human binding molecules described in Table I with the Seq. Id. Nos. pertinent to them but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

6. Claims 1-6, 12, 15, 17, 18 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antibodies described in the Table 1 of the specification, does not reasonably provide enablement for the entire genus of human binding molecules comprising agonistic binding molecules capable of binding to and stimulating a human OX40-receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The instant disclosure fails to meet the enablement requirement for the following reasons:

The invention as claimed, with the exception of the described molecules disclosed in Table I, is not adequately described, as presented supra. There is no guidance and working examples beyond the disclosure related to the molecules described in Table I. Without the appropriate guidance as to the structure of the molecules sought after and based only on the desired functionality of the molecules, a person of ordinary skill in the art would require an undue amount of experimentation to obtain the molecules and then to test them for functionality. Therefore, only the claims are enabled only for the molecules described in Table I of the specification but not for the full scope.

Claim 2 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antibodies denominated SC02-008, SC02-023, does not reasonably provide enablement for other types of molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of

experimentation needed to make or use the invention. In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claim is drawn to human binding molecules comprising agonistic binding molecules capable of binding to and stimulating a human OX40-receptor, wherein the binding molecule has a synergistic stimulatory effect when co-incubated with OX40-ligand. The art was aware of agonistic antibodies against OX40-receptor but the antibodies that bind OX40-L and have a synergistic effect when co-incubated with OX-40L were not known and a person of ordinary skill in the art could not have been able to predict which antibody might have this property without extensive experimentation. The working examples disclosed in the specification provide enablement only for the antibodies denominated SC02-008 and SC02-023 but not for the other antibodies disclosed. Therefore, it is considered that, because of the large quantity of experimentation necessary to generate the unknown number of potentially agonistic binding molecules recited in the claims and possibly screen the same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity; the absence of working examples directed to same; the state of the prior art which establishes the unpredictability of the synergy required by the claims; undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Weinberg AD. (U.S. Pat. No. 6,312,700, 11/6/2001 –cited by the Applicant).

Weinberg teaches OX-40 receptor binding agent selected from OX-40L, anti-OX-40 antibodies (e.g. a monoclonal antibody such as a humanized monoclonal antibody), and immunologically effective portions of anti-OX-40R antibodies that stimulate the activity of the OX-40R. The purified OX-40 receptor binding agent and a pharmaceutically acceptable carrier can be used in the manufacture of a pharmaceutical composition for enhancing the immune response of a mammal (col. 2, line 60 to col. 3 line 2). Another human binding molecule capable of binding OX40R is OX-40L:HuFcIgG in which the extracellular domain of OX-40L is fused to the heavy chain of human IgG. The fusion protein OX40L:huFcIgG was expressed in the well-known CHO cell expression system, using G418 selection and the known pGEM-T cloning vector system (col. 9, line 61 to col. 10, line 54).

Thus the teachings of Weinberg et al anticipate the claims 1 and 12. /Lorraine Spector, Ph.D./

Primary Examiner, Art Unit 1647

9. Claims 1 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Godfrey et al. (U.S. Pat. No. 5,821, 332, 10/13/1998–cited by the Applicant).

Godfrey et al. teach humanized antibodies that bind and stimulate the human Act-4 receptor (which is a synonym for the OX40-R) (col. 2, Line 66 to col. 3, line 30). Production of human antibodies is described by three different methods that address the limitations of claim 12 (col. 15, lines 30 to col. 17, line 35). Therefore the teachings of Godfrey et al. anticipate the claims 1 and 12 of the instant Application.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

- Weinberg AD, (WO/99/42585, 08/29/1999–cited by the Applicant) discloses the use of murine OX-40R agonistic Ab or of OX-40L for enhancing T-cell activation in vitro and the in vivo immune response to tumor cells in humans. The Ab or ligands may be provided in nucleic acid form as well. Anti-OX40 binding agents are capable of stimulating T cells in vitro and to protect animals from tumors in vivo. Accordingly, the data suggest that OX-40R based therapy can generally enhance the immune system.
- Vaughan et al. (Nature Biotechnology, 16, 535-539, 1998–cited by the Applicant) describes the state of the art (1998) in obtaining human antibodies.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/ Ph.D.

Primary Examiner, Art Unit 1647